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Subject: Request for External Peer Review of a Draft Amendment to the Recycled Water Policy regarding monitoring requirements for constituents of emerging concern (CECs)in recycled water and the report "Monitoring Strategies for Chemicals of Emerging Concern (CECs) in Recycled Water – Recommendations of a Scientific Advisory Panel", which is the scientific basis of the recycled water policy amendment.

(1) Sufficiency of potential water contaminant lists of CECs (chemicals of emerging concern).

The list of chemicals that will be monitored according to Amendment A, namely four compounds as indicators of human health-relevant CECs, six performance indicator CECs (two of which overlap with a health-relevant CECs) and a list of potential surrogates from which the most relevant compounds will be chosen, seems to be predicated on relatively minimal data. This is well recognized by the Science Advisory Panel Report from 2010. As a result of this concern, in addition to suggesting the list of compounds that have been incorporated into the Amendment A from 2012, the Panel suggested that the State perform literature reviews to determine which contaminants have been detected in other geographical

locals as well as predicting which chemicals may be predicted to be important from production/release perspective, that State Agencies continue to develop methods for additional contaminants that may be found in recycled water, and that it may be appropriate to perform bioassays to examine particular endpoints that may be caused by various endpoints of interest. This last suggestion would complement the measurement of the specific compounds, for example, if N-nitrosodimethylamine were measured in the water at various monitoring points and a mutagen assay such as the Ames test were also performed at the same monitoring points, it would show if the N-nitrosodimethylamine was representative of the whole category of mutagenic substances. This aspect of the Science Advisory Panel 2010 Report appears to have been omitted in the 2012 Amendment (or Amendment A only covers a portion of the Panel's recommendations). Additionally, there was a suggestion by the Panel Report (2010) that three additional compounds be monitored to establish MECs, namely 1,2,3-trichloropropane, hydrazine and quinoline (pages 72-73). Again, this suggestion is not incorporated in the 2012 Amendment.

One category of compounds that is not mentioned in the report (so it is not clear to the Reviewer if it could potentially be an issue or has been ruled out) are the prokaryotic toxins (E. Valerio, S Chaves, R. Tenreiro. Diversity and impact of prokaryotic toxins on aquatic environments: A review. Toxins 2: 2359-2410, 2010). This category of compounds includes cyanotoxins that could develop secondarily as a result of the nutrient load from wastewater that is released to holding ponds prior to groundwater recharge. This category of compounds is listed in the 2010 Panel Report in Appendix D (Table D-1), although it is listed in the Table along with specific chemical entities, but in this instance refers to CECs that may be relevant to drinking water that can be derived from surface water. The Reviewer is not sure if these compounds could be of concern (perhaps if nutrient-rich wastewater was released into holding ponds that were able to support cyanobacteria), but it is certain that the wide diversity of different compounds in this category are probably not well represented by the compounds chosen for monitoring.

Another category of compounds that is not represented on the list of proposed monitored compounds are inorganic compounds. The 2010 Panel Report mentions boron, chlorate and gadolinium in this category of compounds. Also, tables in the 2010 Report list chromium VI, vanadium, and manganese as potential drinking water CECs. The Reviewer would suggest that lithium might also be a chemical of concern based on its use as a pharmaceutical agent at relatively high dosages.

I would contend that this particular issue, namely the choice of chemicals to monitor, is the primary concern regarding health effects of recycled water. That is why the Science Advisory Panel suggested a wide variety of activities to attempt to supplement and refine the list of monitored chemical agents. Additionally, it was suggested that additional panels be appointed to continue to address this issue because for the foreseeable future the process of evaluating this list should be a dynamic, as opposed to static, process.

The original Science Advisory Panel suggested extensive use of bioassays to monitor biological activity with the idea that analytical capability to monitor thousands of compounds would be limiting for detecting all of the contaminants in recycled water. Furthermore, this

approach would allow an assessment of the interaction of compounds which may be non-additive for a particular biological endpoint. Although the Reviewer recognizes the value of this approach as indicated previously in the case of monitoring N-nitrosodimethylamine and mutagenic compounds, he also has concerns with respect to this approach. It is thought that it will be difficult to predict which biological endpoints to monitor. The Panel suggests that evaluating mutagenic and estrogenic compounds would be valuable endpoints, but this only represents a couple of potential endpoints for which there may be hundreds or thousands. Thus, in addition to the suggestions in the Science Advisory Panel Report (2010), the Reviewer would suggest some general chemical screens of either gas chromatographic or liquid chromatographic separations coupled with mass spectrometry to attempt to determine the number of unknowns in recycled water (and some preliminary idea of the relative quantities of the unknowns).

(2) Appropriateness of the approach for selecting CECs of toxicological relevance to monitor for recycled water uses.

(a) Compilation of CEC occurrence data for municipal recycled water in California (MEC)

If the first issue, sufficiency of the potential water contaminant list, is the most critical issue for determining the potential hazard from recycled water, then the compilation of the chemicals that are in the water is an essential database for determining the sufficiency of the contaminant list. A comprehensive list of the chemical compounds that are found in recycled water as well as the quantity of the compounds would be an extremely valuable data source for determining the most toxic chemical agents. However, the collection of this data is just beginning. For years, the concentrations of pharmaceutical agents and personal care products were not measurable in water, but due to increased population pressures which causes a decrease of natural attenuation time coupled with increased analytical capability, these compounds can now be detected routinely in surface waters. For many years, there has been a realization that the chlorination process produces trihalomethanes, haloacetic acids and dihaloacetonitriles, but only relatively recently has it been determined that nitrosamines are also produced by this process. This is a significant finding because nitrosamines are significantly more potent carcinogens than the other categories of compounds. So, a significant amount of effort should be attributed to determining the vast number of contaminants that are found in water and developing analytical techniques to measure the concentrations of the compounds in aquatic systems. Because this is such a large task, it would be beneficial to coordinate efforts to perform this process with other agencies that may be interested in this data such as the U.S. EPA and the U.S. Geological Survey as well as other states that are interested in determining the purity of drinking water as well as recycled water.

Although measured environmental concentrations (MECs) of the contaminants in water are the ultimate goal, the Science Advisory Panel Report (2010) suggested that predicted environmental concentrations (PECs) could be derived by using information regarding the amount of various contaminants that are purchased and estimating the amount that could find their way into wastewater. This would be a difficult exercise in prediction, but may yield information that would be valuable in prioritizing analytical development approaches. This approach could use information regarding the environmental half-life of chemical substances

as well as data on the human half-life and various physicochemical parameters to hypothesize which compounds should be detectable in aquatic environments, and then subsequent studies could verify the predictions.

(b) Assignment of a toxicologically relevant concentration level, referred to as an initial monitoring trigger level (MTL), to individual CEC for each recycled water exposure scenario.

From a toxicological perspective, it may be anticipated that concentrations of chemicals causing toxicological endpoints will be constantly decreasing as scientists become more and more sophisticated in the ability to detect subtle toxic endpoints. However, the use of the MTL in this instance is a method of prioritizing chemicals so that the presumably more toxic agents are evaluated first. The use of MTLs to reduce the entire toxicity profile to a single value may be objectionable to some toxicologists, but it certainly serves a purpose in this instance. It does not seem appropriate to refer to the MTL as a toxic level. The MTL is actually derived from the allowable daily intake (ADI) of the compound, and consequently is probably more appropriately defined as a safe level of a specific contaminant. Clearly, ADIs are designed to describe a biological response of the general population, and there will be instances where genetic susceptibilities will make an individual sensitive to an agent that is non-toxic to the general population.

One of the major concerns of this overall process which produces a ratio of the environmental concentration of an aqueous contaminant (MEC) to the "monitoring trigger level" (MTL) which is somewhat of a conservative surrogate for a toxic concentration of the compound, is the validity of the MTL value. The proposed process for calculating the MTL is to use the screening level allowable daily intake (ADI) to calculate the MTL. The Panel Report (2010) describes large variability (a factor of 2000-fold) in the ADI for 17β-estradiol. This same issue is mentioned later in the Report (Section 8.2) where it is stated that the reason that the MEC to MTL ratio exceeded 1.0 for 17β-estradiol was because the MTL was based on data from the California Office of Environmental Health Hazard Assessment (OEHHA) cancer slope factor as opposed to the ADI developed by the World Health Organization (WHO). Such a lack of consistency in the calculated MTLs, undermines the entire process of creating an MEC to MTL ratio as the primary parameter for determining the course of action for a contaminant.

(c) Comparison of the MEC to the MTL.

In general, the concept of using a ratio of environmental concentrations (MEC) to concentrations of concern (MTL) seems logical to the Reviewer. It also seems logical that the Science Advisory Panel Report (2010) states that in the absence of environmental concentrations, prioritization of compounds will be on those agents that are the most potent (defined as compounds with an MTL less than or equal to 500 ng/liter).

The risk assessment approach that is summarized on page 31 of the Science Advisory Panel Report (2010) is derived from the Executive Summary of Snyder et al (2010). The Reviewer

was unable to obtain this reference which presumably rationalizes the simple, conservative approach devised by the authors in consultation with outside experts. Consequently, there are some issues that are not explained in the 2010 Report that may be explained in the Snyder et al. reference. So with the caveat that the risk assessment procedure has been designed by more qualified individuals than myself and may be rationalized in the Snyder et al reference, the issues are as follows:

(1) Essentially, the proposed approach uses the therapeutic dose equivalently to the lowest observed adverse effect level (LOAEL), thus assuming a therapeutic index of 1.0. However, the therapeutic index is vastly different for pharmaceutical agents (and is probably available from the US Food and Drug Administration). For example, the therapeutic index for the opioid analgesic reminfentanyl is 33,000 to 1, whereas the cardiac glycoside digoxin has an index of 2 to 1. Is this just a conservative assumption?

(2) The rationale for increasing the uncertainty factor by an order of magnitude for non-genotoxic carcinogens and endocrine disrupting compounds seems somewhat arbitrary. Are the effects of these categories of toxins at low doses more problematic than neurotoxins whose damage may accumulate over a lifetime or immunotoxins that induce a hypersensitivity reaction after a previous exposure?

(d) Evaluation of robust analytical method availability.

It would be valuable from the Reviewer's perspective to know which CECs were removed from consideration because of the lack of commercially available, robust analytical methods. Furthermore, it would be informative to further divide this list of compounds into those that do not have a robust analytical method (a scientific issue) and those for which an appropriate analytical method is just not commercially available (a non-scientific issue). For pharmaceutical agents, for example, it is not clear to the Reviewer why there would not be a robust analytical method, unless the method exists for a biological matrix but requires an extraction procedure for aquatic concentrations.

(3) Determination of initial MTLs for the landscape irrigation.

The assumption that exposure to recycled water through landscape irrigation is 1 percent of drinking water ingestion (20 ml per day) seems to be a reasonable assumption. Thus, the MTLs for landscape irrigation are 100 times higher than the MTLs for potable reuse. Although there are rare scenarios where it may be imagined that children or naïve individuals may exceed this consumption limit, it does not seem reasonable to calculate a conservative consumption value based on these events.

(4) Adequacy of the selected performance indicator CECs.

The Science Advisory Panel Report (2010) suggested the use of six performance indicator CECs: gemfibrozil, nitrosodimethylamine, sucralose, iopromide, caffeine and N, N-diethyl-meta-toluamide. Two of these compounds, caffeine and nitrosodimethylamine, are also

considered CECs based on health criteria. The validity of this list of compounds as indicators of treatment performance will eventually depend on the complete inventory of compounds in recycled water (a constantly changing compendium of compounds) and the capacity of the performance indicators to predict or mimic the other compounds. The Reviewer does not have any better suggestions for compounds on this list, but thinks that the process should be flexible as data is collected and analyzed.

In Attachment 2: Scientific Issues to be Addressed by Peer Reviewers, the following statement is found: "The Panel selected performance indicator CECs based on their high occurrence in recycled water and their ability to be removed by a treatment process that is operating according to its technical specifications." The question is whether there are compounds in recycled water that are not removed by the various unit operations that are currently in place. If such compounds exist, then presumably the performance indicator CECs would fail to predict the fate of such compounds.

(5) Adequacy of the selected surrogates for monitoring treatment process performance.

The Panel Report (2010) suggested a number of surrogate water parameters that may serve as indicators of chemical contaminants including ammonia, nitrate, dissolved organic carbon, UVA spectra, conductivity, turbidity, chlorine residual and total coliform bacteria. The Reviewer does not have the expertise to theoretically predict the relative ability of the surrogate parameters to qualitatively and quantitatively reflect the changes in the concentrations of the CECs. However, the proposed surrogates for landscape irrigation appear to be targeted toward microbiological endpoints. This topic has not been discussed extensively in the Panel Report (2010), although historically it has been a major issue in wastewater reuse. As stated in the Science Advisory Panel Report (2010), a 1998 NRC report recommended that water agencies considering potable reuse fully evaluate the public health impacts from microbial pathogens as well as chemical contaminants. It could include toxins released by microbes as well as spores, conidia, cysts and prions. In addition to CECs are there concerns about microbiological issues?

(6) Validity of expected percent removal of surrogates and performance indicator CECs for a treatment process.

The Reviewer does not have the expertise to evaluate the validity of these estimates. Two CEC compounds appear to exhibit relatively low removal expectations. One is nitrosodimethylamine which is a highly carcinogenic compound and the second is the artificial sweetener sucralose. The relatively low removals for these two compounds, one of which is a known to be highly detrimental to health, brings up the question of whether there are other treatment unit operations which would remove these compounds?

(7) Appropriateness of tiered risk quotient thresholds and corresponding degree of response for evaluating monitoring results for health-based CECs in recycled water.

The tiered risk approach appears to be an overall reasonable approach given the current state

of knowledge in the recycled water field assuming that the MLTs are appropriately determined. There is one aspect of the process that concerns the Reviewer. It is proposed that a specific CEC should be removed from monitoring after a certain number of years (three) if the MEC to MLT ratio remains below 1. The concern is that many of these CECs are continually increasing in the aquatic environment over relatively long time periods and that premature termination of monitoring may prevent the prediction of a future risk. For example, pharmaceutical agents may be constantly increasing in the aquatic environment if their aquatic half-life is long. Thus, it may be prudent to examine the temporal profile of the MEC/MTL value for a compound prior to determining whether to terminate monitoring. For example, if compound X had an MEC/MTL value of 0.1 in the first year of monitoring, a ratio of 0.2 in the second year, and a value of 0.4 in the third year, then it may be appropriate to suggest continued monitoring over time as opposed to discontinuation. In some cases, it may be appropriate to monitor the MEC less frequently, for instance once every three or five years, as opposed to discontinuing monitoring of the compound.

(8) Adequacy of monitoring frequencies for CECs and surrogates and the phased monitoring approach.

It is proposed that the phased monitoring approach will be beneficial in terms of establishing a database in the initial period of the project. For example, sampling every quarter in the first year will allow a determination of whether MEC values demonstrate a seasonal variation as well as facilitating the early collection of a sufficient database to start to determine the variability of the data. Seasonal trends may exist in certain parts of the State but not in others. This is a reason that the overall process should remain flexible.

The Panel Report (2010) proposed "Once every five years, one additional round of CEC monitoring should be conducted to confirm monitoring results." The meaning of this statement is not clear. So, if it is going to be followed, then there should be some guidelines regarding exactly what is going to be confirmed and how this should be done. Does it mean a full scan for a wide variety of compounds, sampling on consecutive days, or taking a single sample and splitting it into two samples? It is not clear as to what is meant by "confirm monitoring results."

(9) Additional consideration for the peer reviews:

It is not clear to the Reviewer, but it appears that wastewater treatment includes both chlorination and advanced oxidation processes (OAP) from Section 1.5.2 in the Science Advisory Panel Report (2010). If the goals of the two unit operations are the same, then there does not appear to be any advantage, and there may be disadvantage, to performing both processes. It would seem that ozone treatment would be an advantageous option when compared to chlorination. It had been known for some time that the ozonation process is just as effective, if not more so, than chlorination in terms of capability to perform disinfection of water. Given that this is the case, the reason that chlorination was favored for disinfection of drinking water was that chlorination produced chloramines which provided longer-term residual disinfection capability that could travel with the water throughout the distribution

system. From this perspective, it would seem that ozonation of wastewater would be preferable to chlorination because the water would not have any residual oxidation capacity that may prevent it from being released to natural water sources in the environment. Residual disinfection capacity for wastewater would be detrimental to its release into natural systems because of potential downstream impacts. Furthermore, since the chlorination process produces a number of potential carcinogens, such as nitrosodimethylamine and trihalomethanes, the elimination of this process would have benefits in terms of reducing the hazardous contaminants in aquatic systems. Prior to making the transition in wastewater disinfection processes from chlorination to ozonation, it would be beneficial to demonstrate that ozonation does not produce more carcinogenic substances than chlorination. A preliminary assessment of this question could be obtained by chlorinating and ozonating wastewater and then extracting the organic fraction from each wastewater and testing the extract in a battery of mutagen assays to compare the relative mutagenicity of the two extracts.

One of the issues that was not discussed comprehensively in the Scientific Advisory Panel Report (2010) was the source of 17β-estrdiol in wastewater. If the majority of the estrogen is excreted from the human (as described in Section 8.2), then have the analyses of wastewater attempted to isolate the natural human metabolites of 17β-estradiol? Compounds of interest could include estradiol and estrone sulfates. Are these metabolites altered in the aquatic environment? Questions regarding additional compounds that have estrogenic activity could be addressed if bioassays of estrogenicity were being used in addition to monitoring 17β-estradiol concentrations.

The Big Picture:

(a) Additional scientific issues

Although not a "Big Picture" item, the Reviewer is unfamiliar with general groundwater practices, and consequently was naïve with respect to how monitoring is performed. The Scientific Advisory Panel Report (2010) stated that for groundwater recharge projects in California, the recharged water is required to remain in the subsurface for a minimum of six months prior to extrapolation. This process would provide an additional level of protection from groundwater contaminants by allowing natural attenuation to occur. How is this monitored?

(b) Taken as a whole is the scientific portion the proposed rule based upon sound scientific knowledge methods and practices?

Yes

(c) Does Attachment A adequately characterize and implement the Panel's recommendations for monitoring of CECs for recycled water use in groundwater recharge and landscape design?

From the perspective of the Reviewer, the recommendations of the Panel included an attempt to gather additional information regarding the identification of CECs. This includes suggestions to look at the greater chemical landscape to determine if all potential wastewater contaminants have been considered (Section 5.3). Although this appears to be an ominous task because there are potentially very large numbers (thousands) of potential wastewater contaminants, available data sources may allow the derivation of predicted environmental concentrations (PEC) that may be the basis for future analytical approaches to transform the PECs into MECs. The Panel Report (2010) also suggested significant literature reviews to identify additional CECs. It is not possible to determine from Attachment A if this task has been performed. Although this process is ominous from the perspective of the total number of potential chemical contaminants, there is some degree of optimism derived from Figure 2.3 in the Panel's Report. This Figure shows a flow diagram for a large number of chemicals in a health effects database. Of 5107 entrees, only 122 of the compounds were considered to be of toxicological concern. Thus, of the large number of contaminants in wastewater, only a small percentage may be of toxicological significance. A second area of Attachment A omission, is the development of bioassays to monitor various biological endpoints in the wastewater treatment process (Section 6.0). Finally, the Panel suggests monitoring for additional CECs with insufficient MECs (Section 8.5), including 1,2,3-trichloropropane, hydrazine and quinolone. Thus, the Reviewer found the original Report by the Scientific Advisory Panel (2010) was considerably more broad-based than the Attachment A proposed aims.